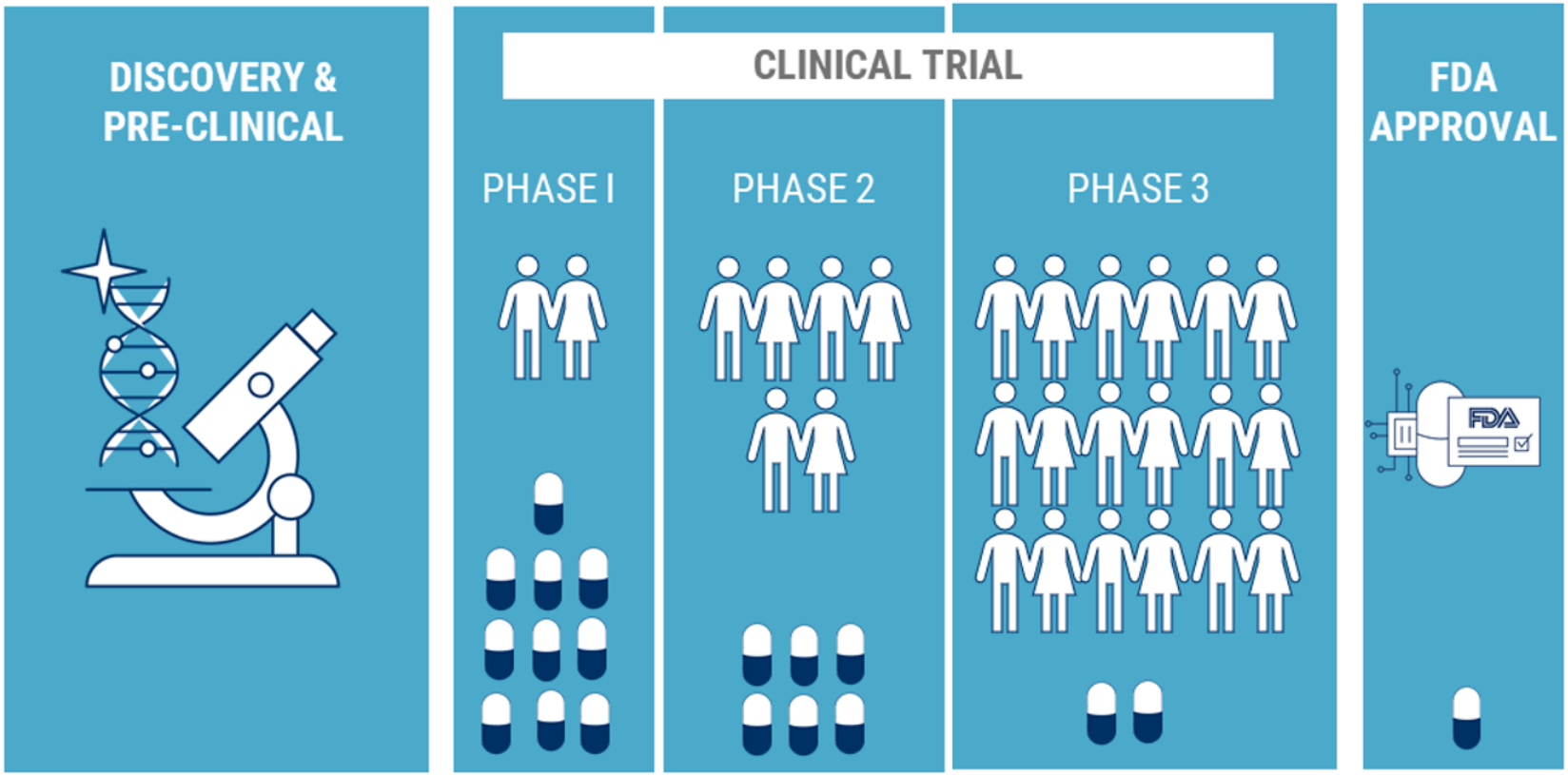
Dott.ssa Monica Tani
U.O.C Ematologia
Ravenna

Sviluppo della ricerca di Fase I a Ravenna nelle neoplasie ematologiche

Sperimentazioni Cliniche



Source: cbinsights.com

CBINSIGHTS

I PRINCIPALI DETERMINANTI DELLA COMPETITIVITÀ E DELLA ATTRATTIVITÀ

Tabella 2 - Criteri adottati dalle imprese per la selezione dei Paesi e dei Centri in cui condurre attività di ricerca clinica (3)

1. Dimensioni del Mercato	• *Popolazione* • *Incidenza delle patologie* • *Consistenza obiettivi di reclutamento* • *Dimensione del mercato (domanda)*
2. Efficienza	
a. Pianificabilità	• *Costanza, standardizzazione e certezza dei tempi di risposta dei diversi Centri nel Paese* • *Percentuale di centri attivi negli studi ma non arruolanti* • *Capacità di arruolamento dei centri*
b. Tempestività	• *Start up d… …volti nel Paes…* • *Tempi di…*
c. Qualità del Dato	• *Costi del…* • *Queries* • *Dati non…*
d. Costi	• *Costo de…* • *Costo pe…*
3. Qualità	
a. Risorse	• *Qualità de…* • *Esperienza dello staff* • *Meccanismi di coinvolgimento dello staff nello studio* • *Reputation e competenze dello sperimentatore principale* • *Proattività sperimentatore principale*
b. Strutture	• *Qualità nelle cure* • *Qualità nella gestione dei documenti fonte* • *Location* • *Coordinamento tra sperimentatori e Comitato Etico*
c. Meccanismo Operativi	• *Aderenza al protocollo* • *Raccolta consenso informato* • *Registrazione Eventi Avversi*
d. Gestione del Farmaco	• *Procedure di gestione del farmaco: conservazione, dispensazione* • *Adeguatezza strutturale della farmacia*

STRUTTURE ACCREDITATE FASE I

1.2 MLN ABITANTI

ATTENDIBILITÀ PREVISIONE ARRUOLAMENTO

CONVENZIONI NEGOZIATE ENTRO CEROM: >80%

UNICO CE , UNICA CONVENZIONE

SISTEMA INFORMATIVO

COLLABORAZIONE CON CRO: PIANIFICAZIONE VISITE, DISPONIBILITÀ TEAM, LOG80, SPAZI DEDICATI

QUALITÀ, PRESENZA UBSC = PERSONALE QUALIFICATO

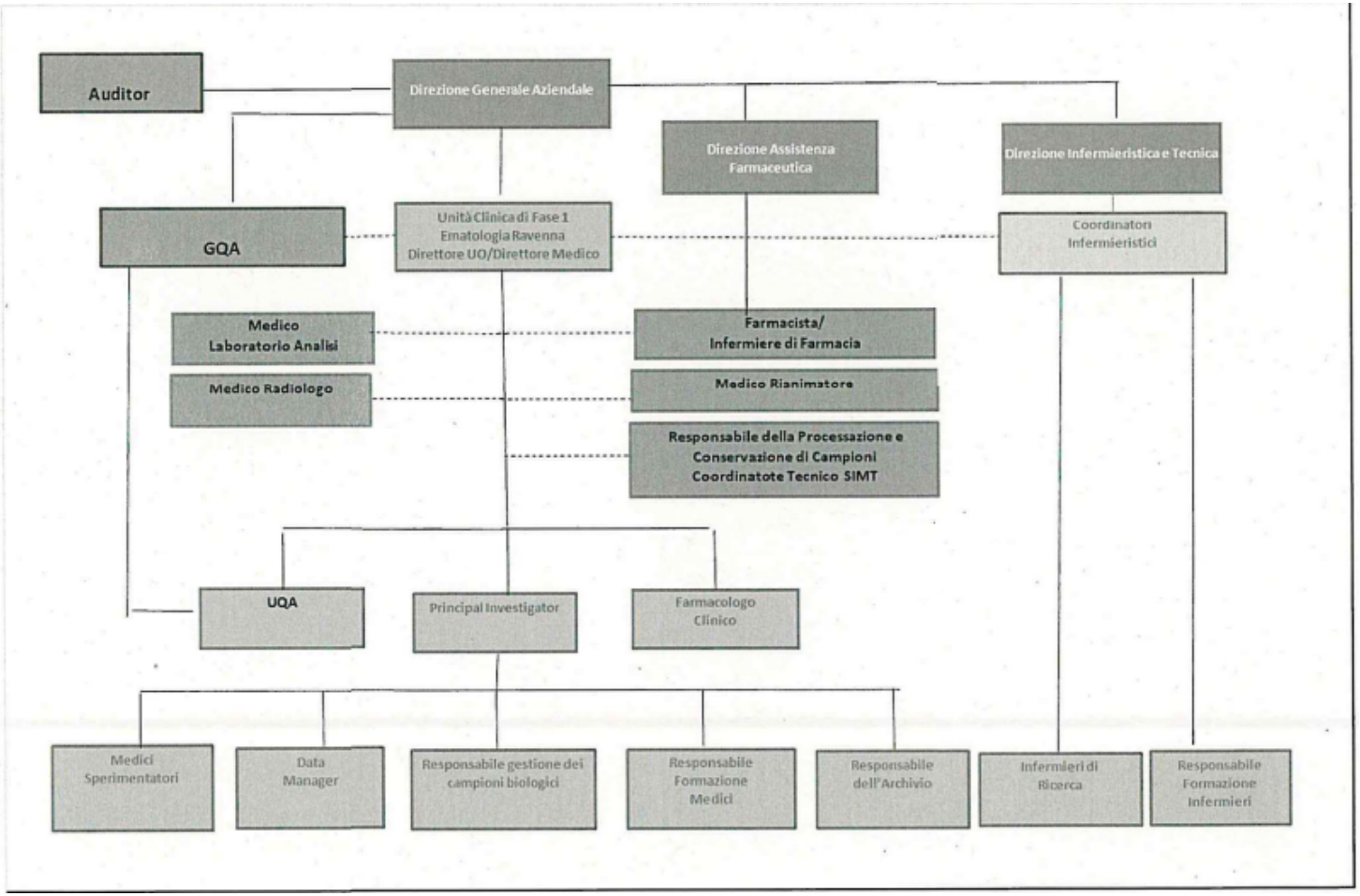
Fonte: Rap…

STRUTTURE ACCREDITATE PER FASE I

	AUSL DELLA ROMAGNA	LABORATORIO DI FASE I (c/o LABORATORIO A RISPOSTA RAPIDA FORLI')	Laboratorio di analisi	Pazienti	Forlì	FC	19/06/2017
	AUSL DELLA ROMAGNA	LABORATORIO DI FASE I (c/o LABORATORIO A RISPOSTA RAPIDA RAVENNA)	Laboratorio di analisi	Pazienti	Ravenna	RA	19/06/2017
	AUSL DELLA ROMAGNA	LABORATORIO DI FASE I (c/o LABORATORIO A RISPOSTA RAPIDA RIMINI)	Laboratorio di analisi	Pazienti	Rimini	RN	19/06/2017
	AUSL DELLA ROMAGNA	LABORATORIO DI FASE I (c/o UO MICROBIOLOGIA PIEVESESTINA - CE)	Laboratorio di analisi	Pazienti	Pievesestina	FC	19/06/2017
	AUSL DELLA ROMAGNA	LABORATORIO DI FASE I (c/o UO PATOLOGIA CLINICA PIEVESTESTINA - CE)	Laboratorio di analisi	Pazienti	Pievesestina	FC	19/06/2017

	STITUTO SCIENTIFICO ROMAGNOLO PER LO STUDIO E LA CURA DEI TUMORI S.R.L. IRCCS	UNITA' CLINICA DI FASE I	Centro clinico	Pazienti	Meldola	FC	20/10/2016
	OSPEDALE INFERMI DI RIMINI	UNITA' CLINICA DI FASE I CARDIOLOGIA RIMINI PRESSO L'U.O. CARDIOLOGIA DI RIMINI	Centro clinico	Pazienti	Rimini	RN	30/03/2017
	OSPEDALE SANTA MARIA DELLE CROCI RAVENNA	UNITA' CLINICA DI FASE I EMATOLOGIA RAVENNA PRESSO L'U.O. EMATOLOGIA DI RAVENNA	Centro clinico	Pazienti	Ravenna	RA	30/03/2017
	OSPEDALE SANTA MARIA DELLE CROCI RAVENNA	UNITA' CLINICA DI FASE I ONCOLOGIA RAVENNA PRESSO L'U.O. ONCOLOGIA DI RAVENNA	Centro clinico	Pazienti	Ravenna	RA	30/03/2017

Organigramma Fase I Ematologia

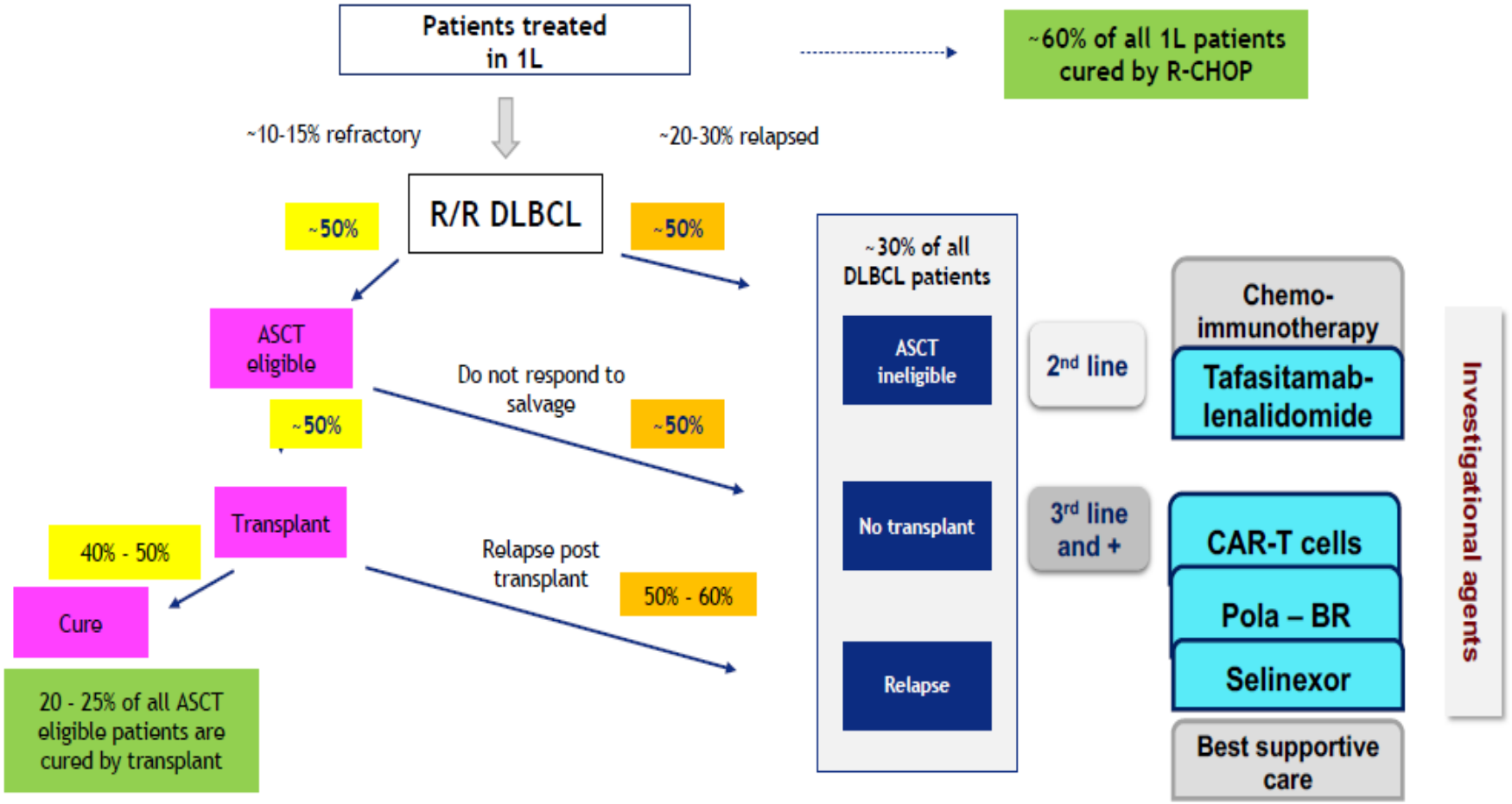


Acronimo	Titolo	Sponsor	Sede	Status Studio	CENTRO	PZ ARRUOLATI
GO29833	A phase Ib/II study evaluating the safety and Efficacy **of obinutuzumab in combination with Polatuzumab vedotin and venetoclax** in Patients with relapsed or refractory Follicular lymphoma and **rituximab in Combination with polatuzumab vedotin And venetoclax** in patients with relapsed or refractory diffuse large b-cell Lymphoma	Roche	FL / DLBCL RR	ATTIVATO NEL 2017	RAVENNA IRST	RAVENNA: 2 FL COORT 2 DLBCL COORT
CITADEL 112	A Phase 1, Open-Label, Dose-Finding Study of **INCB050465** in Combination With Investigator Choice of Rituximab, Bendamustine and Rituximab, or Ibrutinib in Participants With Previously Treated B-Cell Lymphoma.	Incyte	B mal	ATTIVATO NEL 2019	RAVENNA	5
NP 30179	A MULTICENTER, OPEN-LABEL, PHASE I STUDY TO EVALUATE THE SAFETY, EFFICACY, TOLERABILITY AND PHARMACOKINETICS OF ESCALATING DOSES OF GLOFITAMAB (RO7082859) AS A SINGLE AGENT AND IN COMBINATION WITH OBINUTUZUMAB ADMINISTERED AFTER A FIXED, SINGLE DOSE PRE-TREATMENT OF OBINUTUZUMAB (GAZYVA®/ GAZYVARO™) IN PATIENTS WITH RELAPSED/ REFRACTORY B-CELL NON-HODGKIN'S LYMPHOMA	Roche	DLBCL RR/ FL RR/MCL RR	ATTIVATO FEBBRAIO 2019	RAVENNA	8
NP40126	A PHASE 1B STUDY EVALUATING GLOFITAMAB (RO7082859) IN COMBINATION WITH RITUXIMAB (R) OR OBINUTUZUMAB (G) PLUS CYCLOPHOSPHAMIDE, DOXORUBICIN, VINCRISTINE, AND PREDNISONE (CHOP) IN PARTICIPANTS WITH RELAPSED OR REFRACTORY NON-HODGKIN LYMPHOMA (R/R NHL) OR IN PARTICIPANTS WITH UNTREATED DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL)	Roche	DLBCL/FL	ATTIVATO FEBBRAIO 2019	RAVENNA	7
MOR208C107	Phase Ib, open-label, randomized study to assess safety and preliminary efficacy of Tafasitamab in addition to R-CHOP or Tafasitamab plus Lenalidomide in addition to R-CHOP in patients with newly diagnosed Diffuse Large B-Cell Lymphoma (DLBCL) – First-MIND	Morphosys	DLBCL	ATTIVATO DIC 2020	RAVENNA	1

Acronimo	Titolo	Sponsor	Sede	Status Studio	CENTRO	PZ ARRUOLATI
ADCT-402-103	A Phase 1/2 Open-Label Study to Evaluate the Safety and Efficacy of Loncastuximab Tesirine and Ibrutinib in Patients with Advanced Diffuse Large B-Cell Lymphoma or Mantle Cell Lymphoma (LOTIS-3)	ADC Therapeutics	DLBCL RR	ATTIVATO A FEBB 2020	RAVENNA	2 FASE 1 2 FASE 2
CP-MGD006-01	A Phase 1/2, First-in-Human, Dose Escalation Study of MGD006, a CD123 x CD3 Dual Affinity Re-Targeting (DART) Bi-Specific Antibody-Based Molecule, in Patients with Relapsed or Refractory Acute Myeloid Leukemia	MacroGenics	AML	ATTIVATO A MAGGIO 2020	RAVENNA IRST	1 FASE 2
SLN124-002	A randomised, single-blind, placebo-controlled, phase 1, single-ascending and multiple-dose study in adult subjects with alpha/beta-thalassaemia and very low- and low-risk myelodysplastic syndrome to investigate the safety, tolerability, pharmacokinetic, and pharmacodynamic response of SLN124	Silence Therapeutics	MDS LOW RISK alfa/beta TALASSEMIA	ATTIVATO MAGGIO 2021	RAVENNA	0
INCMOR0208-101	A Phase 1b/2a Basket Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of Combination Therapy With the Anti-CD19 Monoclonal Antibody Tafasitamab and the PI3Kδ Inhibitor Parsaclisib in Adult Participants With Relapsed/Refractory Non-Hodgkin Lymphoma or Chronic Lymphocytic Leukemia (topMIND)	Incyte	B malig	ATTIVO SETTEMBRE 2021	RAVENNA	0
BGB-11417-101	A Phase 1/1b Open-Label Dose Escalation and Expansion Study of Bcl-2 Inhibitor BGB-11417 in Patients with Mature B-Cell Malignancies	Beigene	B-cell malig	IN ATTIVAZIONE	RAVENNA	-

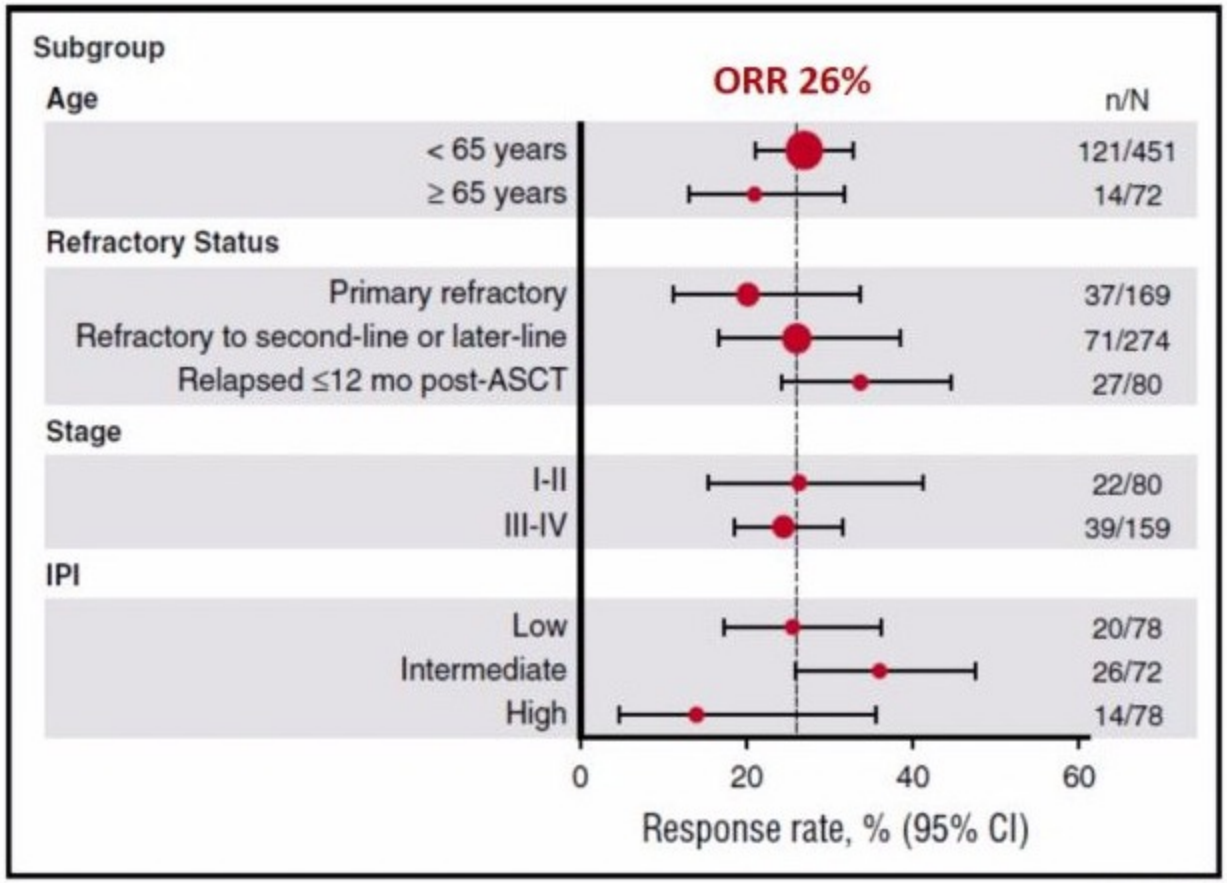
Acronimo	Titolo	Sponsor	Sede	Status Studio	CENTRO	PZ ARRUOLATI
BO42203	A PHASE Ib STUDY EVALUATING THE SAFETY, EFFICACY, AND PHARMACOKINETICS OF VENETOCLAX IN COMBINATION WITH POLATUZUMAB VEDOTIN PLUS RITUXIMAB (R) AND CYCLOPHOSPHAMIDE, DOXORUBICIN, PREDNISONE (CHP) IN PATIENTS WITH UNTREATED BCL-2 IMMUNOHISTOCHEMISTRY (IHC)–POSITIVE DIFFUSE LARGE B-CELL LYMPHOMA	Roche	DLBCL	IN ATTIVAZIONE	RAVENNA IRST	-
KRT-232-113	An Open-Label, Multicenter, Phase 1b/2 Study of the Safety and Efficacy of KRT-232 with TL-895 in Subjects with Relapsed/ Refractory Myelofibrosis and of KRT-232 in Janus-associated Kinase Inhibitor-Intolerant Myelofibrosis	Kartos Therapeutics	MF	IN ATTIVAZIONE	RAVENNA	-

Relapsed and refractory DLBCL



Outcomes in refractory diffuse large B-cell lymphoma: results from the international SCHOLAR-1 study

Michael Crump,[1] Sattva S. Neelapu,[2] Umar Farooq,[3] Eric Van Den Neste,[4] John Kuruvilla,[1] Jason Westin,[2] Brian K. Link,[3] Annette Hay,[1] James R. Cerhan,[5] Liting Zhu,[1] Sami Boussetta,[4] Lei Feng,[2] Matthew J. Maurer,[5] Lynn Navale,[6] Jeff Wiezorek,[6] William Y. Go,[6] and Christian Gisselbrecht[4]



Blood. 2017;130(16):1800-1808

Immunoterapia

Immunoterapia: Il sistema immunitario come approccio al trattamento delle neoplasie

CAR T-cells: linfociti T geneticamente modificati con un recettore diretto contro la cellula tumorale

Anticorpi monoclonali (mAbs): Sfruttano una citotossicità complemento (CDC) e/o anticorpo (ADCC) dipendente

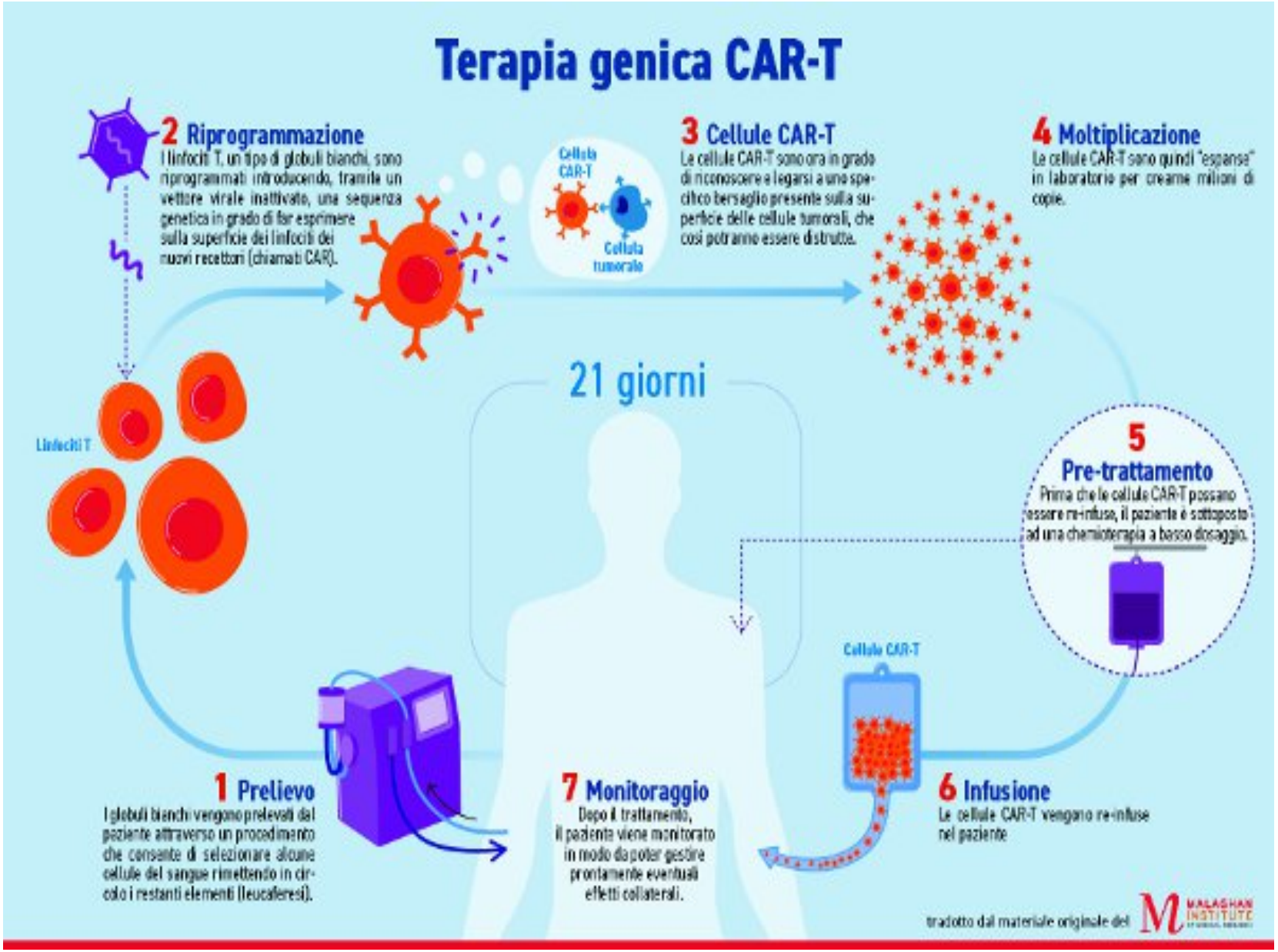
Anticorpi bispecifici (BsAb): anticorpi che legano simultaneamente multipli targets

Es: BiTEs, DARTs, BiKEs

Inibitori dei checkpoint immuni (ICIs): bloccano i regolatori negativi dell'attivazione dei linfociti T

Es: anti PD-1, PD-L1 o CTLA-4

Terapia genica CAR-T



Anti-CD19 CAR T Cell Products for Aggressive B-Cell NHL

	Axicabtagene Ciloleucel (axi-cel)	Tisagenlecleucel (tisa-cel)	Lisocabtagene Maraleucel[e] (liso-cel)
Construct	anti-CD19-CD28-CD3ζ[a]	anti-CD19-41BB-CD3ζ[c]	anti-CD19-41BB-CD3ζ
Vector	Retrovirus[a]	Lentivirus[c]	Lentivirus
T-cell manufacturing	Bulk[b]	Bulk[c]	Defined doses CD4, CD8
Dose	2×10^6/kg (max 2×10^8)[b]	0.1 to 6.0×10^8[d]	DL1: 0.5×10^7 DL2: 1.0×10^8 DL3: 1.5×10^8
Treated / enrolled, n/n (%)	101/119 (91)	111/165 (67)[d]	256/344 (74)
Bridging therapy	None allowed in pivotal trial but often used in standard practice	92%[d]	72%
Lymphodepletion	Flu/Cy 30/500 mg/m^2 × 3 d	Flu/Cy 25/250 mg/m^2 × 3 d, or Benda 90 mg × 2 d[d]	Flu/Cy 30/300 mg/m^2 × 3 d
Approval status	FDA/EMA approved for DLBCL, high grade B-cell lymphoma, transformed FL, PMBCL	FDA/EMA approved for pediatric B-ALL, DLBCL, high grade B-cell lymphoma, transformed FL[c]	FDA approved for R/R large B-cell lymphoma, high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B[f]*

*The FDA approved liso-cel on February 5, 2021, after the taping of this video.

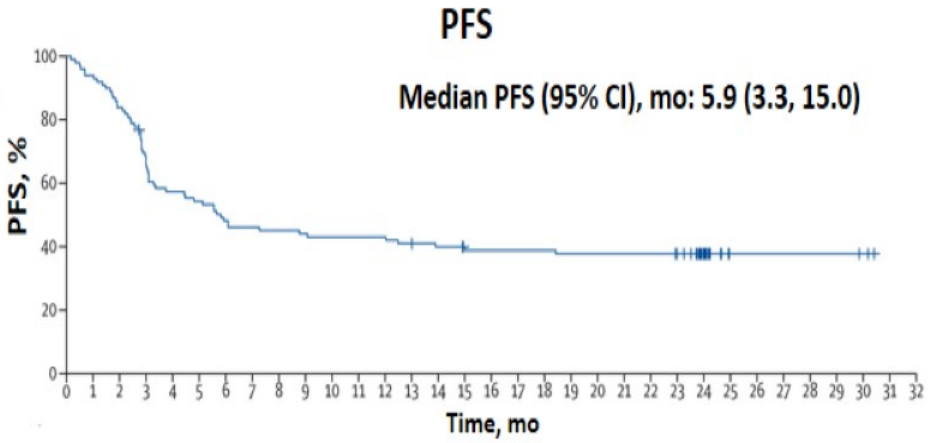
a. Locke FL, et al. *Lancet Oncol*. 2019;20:31-42; b. YESCARTA™ (axicabtagene ciloleucel) [PI]. 2017; c. KYMRIAH™ (tisagenlecleucel)[PI]. 2017; d. Schuster SJ, et al. *N Engl J Med*. 2019;380:45-56; e. Abramson J, et al. *Lancet*. 2020;396:839-852; f. FDA. News release. February 5, 2021.

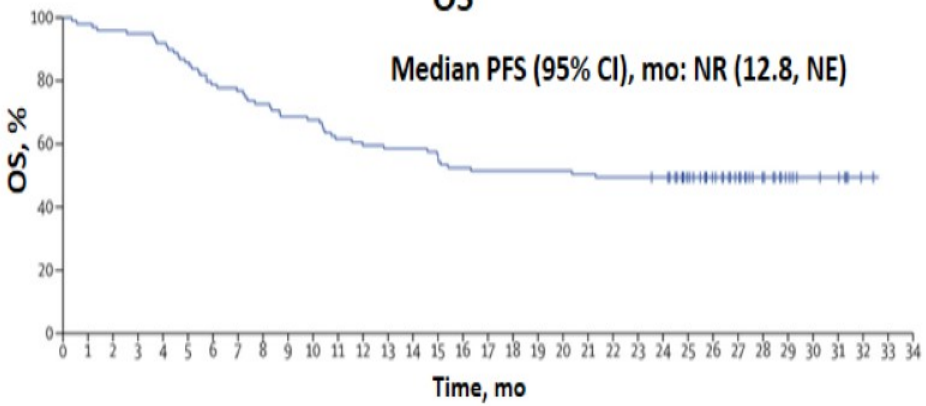
ZUMA-1

Axi-Cel in Patients With R/R LBCL

Patient Characteristics	Phase 1 and 2 (N = 108)
Median age, y	58
Age ≥ 65 y, n (%)	27 (25)
Disease stage III/IV, n (%)	90 (83)
IPI risk score 3 or 4, n (%)	48 (44)
≥ 3 prior therapies, n (%)	76 (70)
Refractory to 2nd- or later-line therapy, n (%)	80 (74)
Best response as PD to last prior therapy, n (%)	70 (65)
Relapse post ASCT, n (%)	25 (23)

- ORR (n = 101), % [by IRC]: 83 [74]
- CR, %: 58
- CRS (%): Any (93); Grade ≥ 3 (11)
- Neurotoxicity (%): Any (64); Grade ≥ 3 (32)

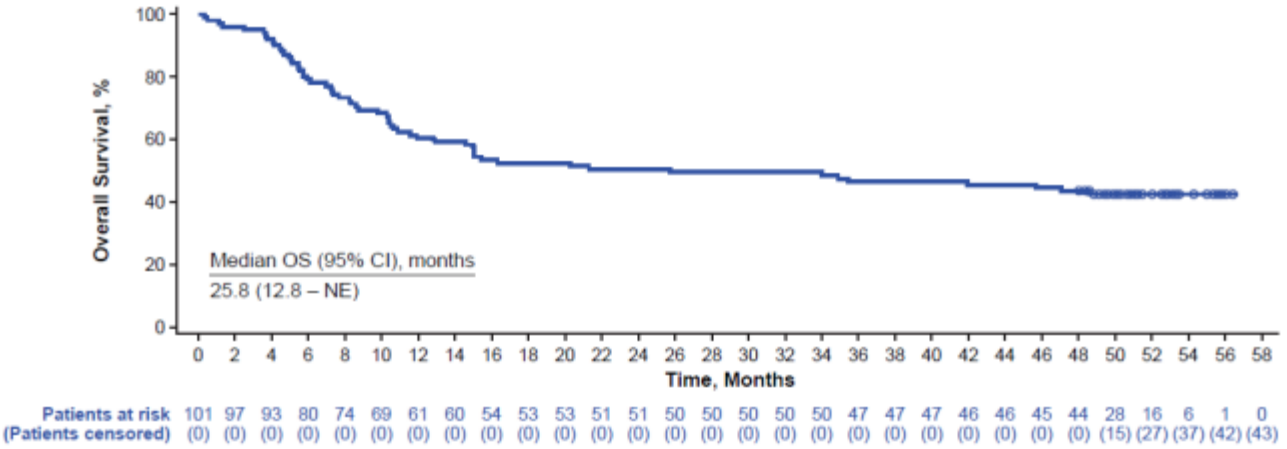




Locke FL, et al. *Lancet Oncol*. 2019;20:31-42.

Zuma-1 Follow-up 4 aa

Overall Survival At 4 Years (mITT, n = 101)



- Among axi-cel–treated patients (mITT, n = 101), with ≥ 4 years of follow-up (median, 51.1 months), median OS was 25.8 months, and the KM estimate of the 4-year OS rate was 44%
- Among the entire enrolled population (ITT, n = 111), median OS was 17.4 months, and the KM estimate of the 4-year OS rate was 41%

axi-cel, axicabtagene ciloleucel; KM, Kaplan-Meier; mITT, modified intent-to-treat; NE, not estimable; OS, overall survival.

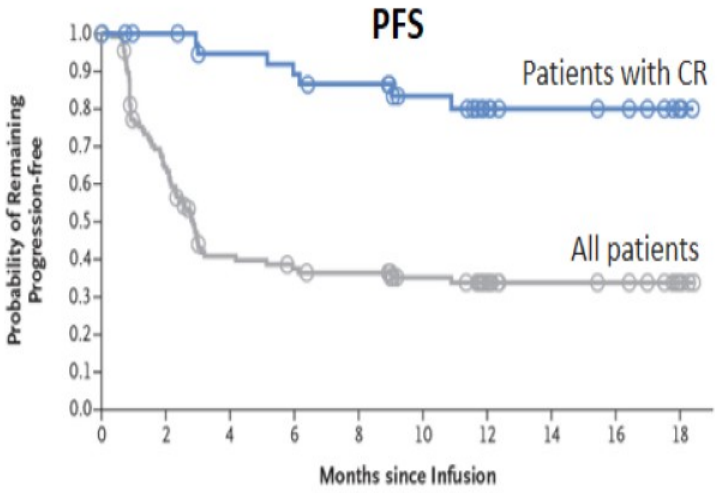
Jacobson et al ASH 2020 Abstract 1187

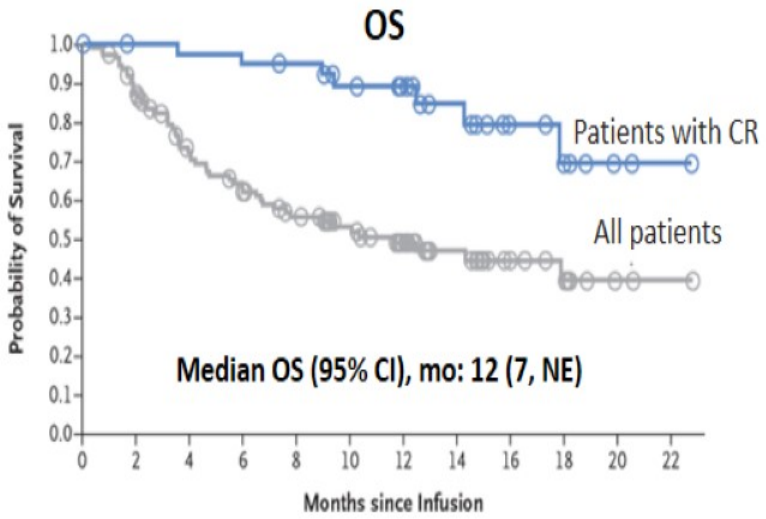
JULIET

Tisa-Cel in Patients With R/R DLBCL

Patient Characteristics	Phase 1 and 2 (N = 111)
Median age (range), y	56 (22-76)
Double- / triple-hit lymphoma, %	27
No. of prior lines of therapy, %	
2	44
3	31
4-6	21
Refractory to last therapy, %	55
Prior ASCT, %	49

- ORR, %: 52
- CR, %: 40
- CRS (%): Any (58); Grade ≥ 3 (22)
- Neurotoxicity (%): Any (21); Grade ≥ 3 (12)*





*Penn scale.

Schuster SJ, et al. *N Engl J Med*. 2019;380:45-56.

TRANSCEND-NHL-001

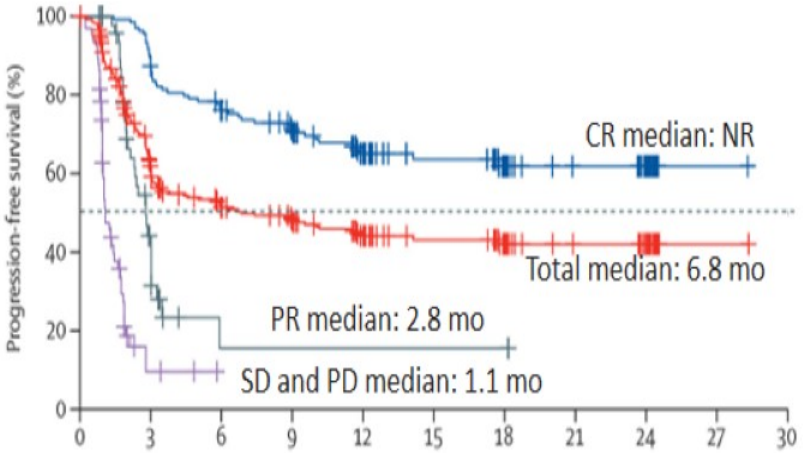
Liso-Cel in Patients With R/R LBCL

Patient Characteristics	Patients (N = 269)
Median age (range), y	63 (54-70)
Double- / triple-hit lymphoma, n (%)	36 (13)
CNS involvement, n (%)	7 (3)
Median prior lines, n (range)	3 (2-4)
Chemo-refractory, n (%)	181 (67)
Prior HSCT, n (%)	94 (35)

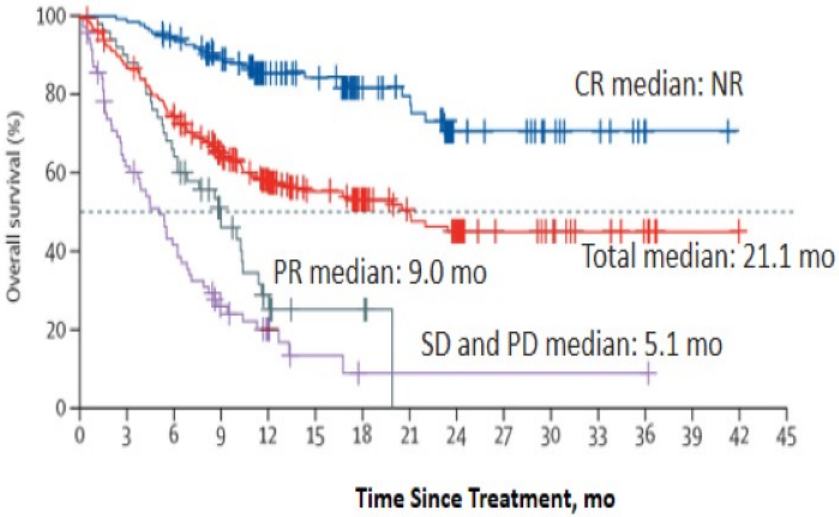
Best Response	Patients (N = 256)
Best Objective response rate, %	73
Best CR, %	53
12-month DOR, %	55

- CRS (%): Any (42); Grade ≥ 3 (2)
- Neurotoxicity (%): Any (30); Grade ≥ 3 (10)

PFS



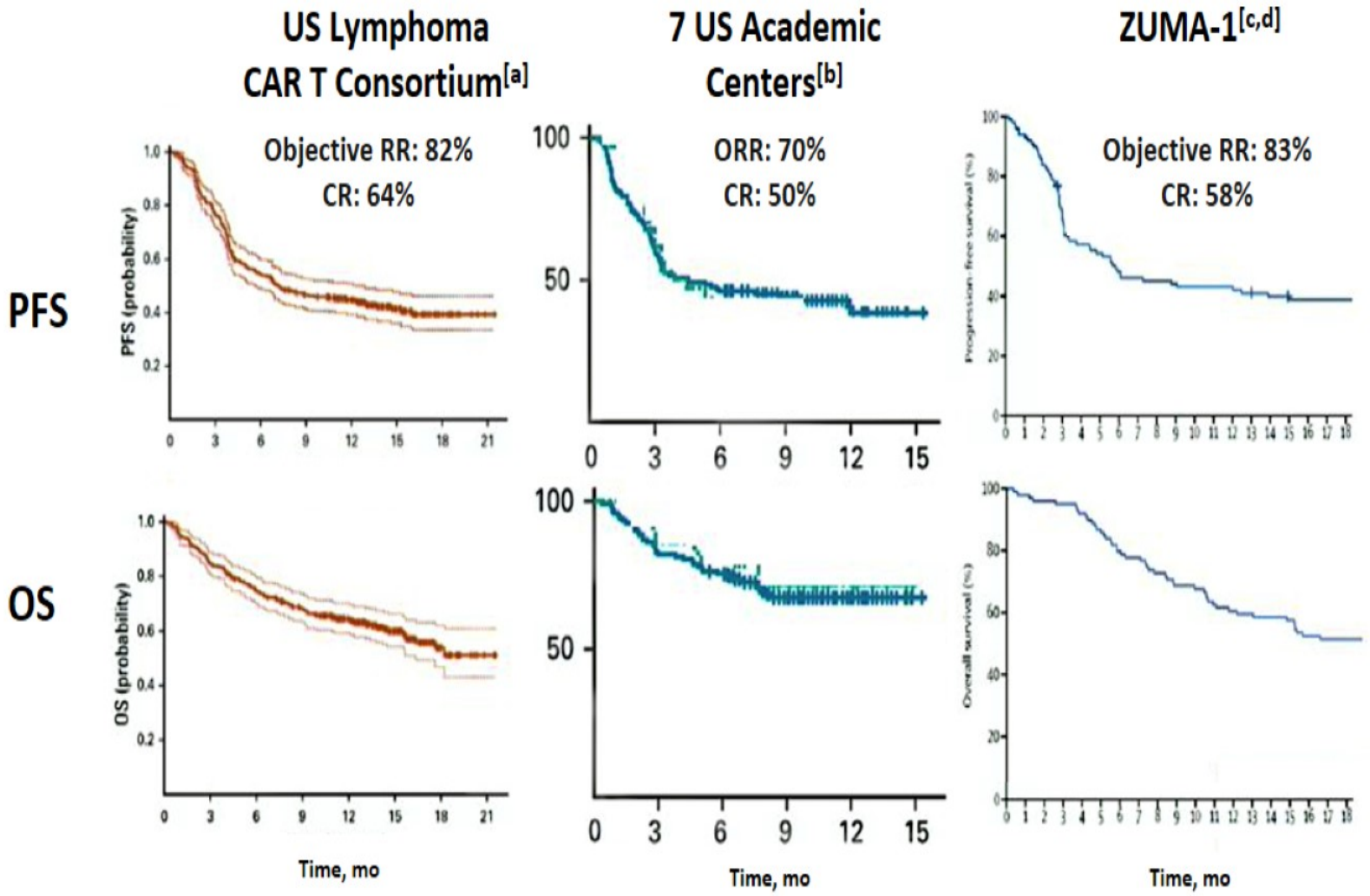
OS



Abramson JS, et al. *Lancet*. 2020;396:839-852.

2 Real-World Studies vs ZUMA-1

Survival and Response Rates



a. Nastoupil LJ, et al. *J Clin Oncol*. 202020;38:3119-3128; b. Jacobson CA, et al. *J Clin Oncol*. 2020;38:3095-3106; c. Neelapu SS, et al. *N Engl J Med*. 2017;377:2531-2544; d. Locke FL, et al. *Lancet Oncol*. 2019;20:31-42.

Tossicità specifiche

✓**Sindrome da rilascio di citochine (CRS)**

- **Risposta infiammatoria sistemica causata da rilascio di citochine**
- **Si manifesta come febbre, ipotensione, desaturazione e tossicità d'organo**

✓ **Neurotossicità (ICANS)**

- **Legata alla diffusione passiva di citochine nel SNC**
- **Si manifesta con disorientamento spazio temporale, afasia, edema cerebrale nelle forme severe**

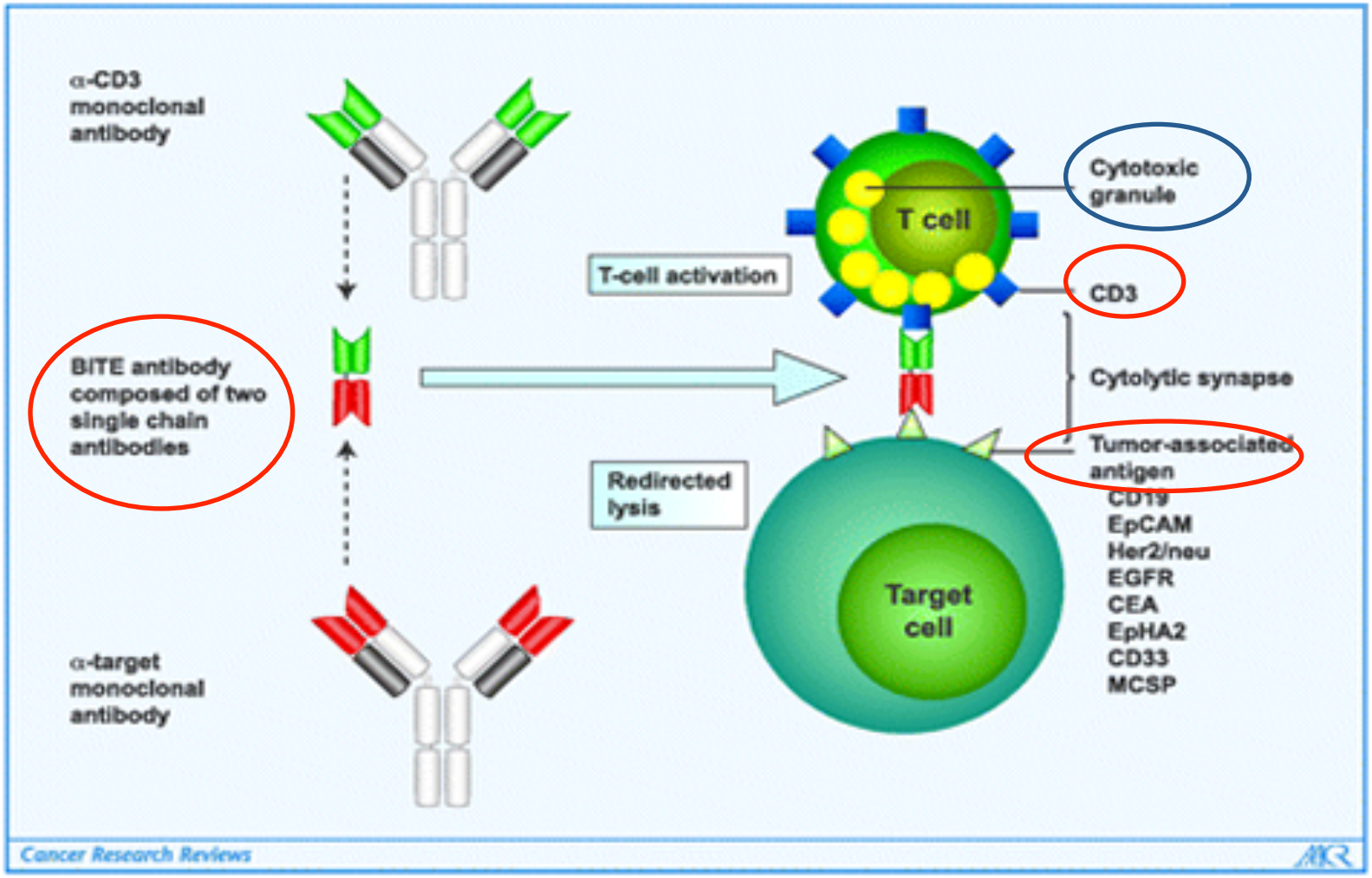
2 Real-World Studies vs ZUMA-1

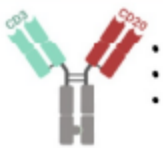
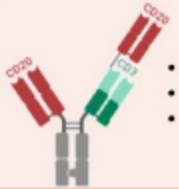
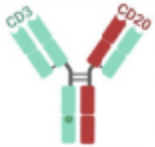
Patient Characteristics

	US Lymphoma CAR T Consortium[a]	7 US Academic Centers[b]	ZUMA-1[c,d]
N (dosed)	298 (275)	122 (N/A)	111 (101)
Median age, y (range)	60 (21-83)	62 (21-79)	58 (23-76)
LDH > normal at lymphodepletion, %	61	40	N/A
Prior ASCT, %	33	25	23
Bridging, %	53	45	0
Bulky disease >10 cm, %	23	14	17
ECOG ≥ 2, %	19	10	0
ZUMA-1 ineligible, %	43	62	0

a. Nastoupil LJ, et al. *J Clin Oncol*. 2020;38:3119-3128; b. Jacobson CA, et al. *J Clin Oncol*. 2020;38:3095-3106; c. Neelapu SS, et al. *N Engl J Med*. 2017;377:2531-2544; d. Locke FL, et al. *Lancet Oncol*. 2019;20:31-42.

Bispecific T-cell engagers(BiTEs)



Bi-Specific Antibody	Targets	Design	Ig Fragment Formats	Ref.
blinatumomab	**CD19 x CD3**		• two murine scFv joined by a glycine-serine linker • monovalent CD19 and monovalent CD3 binding • cloned from anti-CD19 (clone HD37) and anti-CD3 (clone L2K-07) murine mAbs	1, 2, 3
mosunetuzumab	**CD20 x CD3**		• humanized mouse heterodimeric IgG1-based antibody • monovalent CD20 and monovalent CD3ε binding • modified Fc devoid of FcγR and complement binding	4
glofitamab	**$(CD20)_2$ x CD3**		• humanized mouse IgG1-based antibody • bivalent CD20 and monovalent CD3ε binding • modified Fc devoid of FcγR and complement binding	5
odronextamab	**CD20 x CD3**		• fully human IgG4-based heterodimeric antibody • monovalent CD20 and monovalent CD3ε binding • Fc-dependent effector function-minimized antibody with Fc of the anti-CD3ε heavy chain modified to reduce Protein A binding • common κ light chain from anti-CD3ε mAb	6
epcoritamab	**CD20 x CD3**		• humanized mouse IgG1-based heterodimeric antibody • monovalent CD20 and monovalent CD3 binding • IgG1 Fc modified to minimize Fc-dependent effector functions and to control Fab-arm exchange of mAb half-molecules, resulting in high bispecific product yield	7

Ig, immunoglobulin; scFv, single-chain variable fragment; mAb, monoclonal antibody; Fc, fragment crystallizable; FcγR, Fc gamma receptor

[1]Dufner V, *et al*. Blood Adv (2019) 3:2491; [2]Goebeler ME, *et al*. J Clin Oncol (2016) 34:1104; [3]Viardot *et al*. Blood (2016) 127(11):1410; [4]Schuster SJ, *et al*. ASH 2019, Plenary Abstract 6; [5]Hutchings M, *et al*. ASH 2020, Abstract 403; [6]Bannerji R, *et al*. ASH 2020, Abstract 400; [7]Hutchings M, *et al*. ASH 2020, Abstract 406

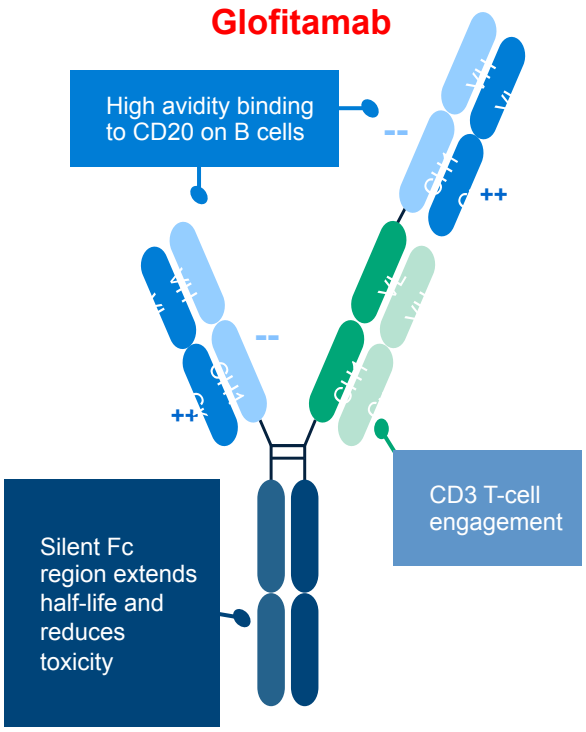
Bi-Specifics CD3 x CD20 in patients with DLBCL: update at ASH 2020

	Mosunetuzumab[1] (RG7828)	Odronextamab[1] (REGN1979)	Glofitamab[1] * (RG6026)	Epcoritamab[1] (GEN3013)
Patients	98	35	28	33
ORR	38%	40%	61%	76%
CR	20%	31%	54%	48%

1. Schuster SJ et al, ASH 2019, Abstract 6 (doses >=2.5 mg); 2. Bannerji R, et al. ASH 2020, Abstract 400 (doses 80-320); 3. Hutchings M, et al. ASH 2020, Abstract 403 (step up dosing from 2.5 to 16/30 mg); 4. Hutchings M, et al. ASH 2020, Abstract 402 (all doses).
2. * "aggressive lymphoma"

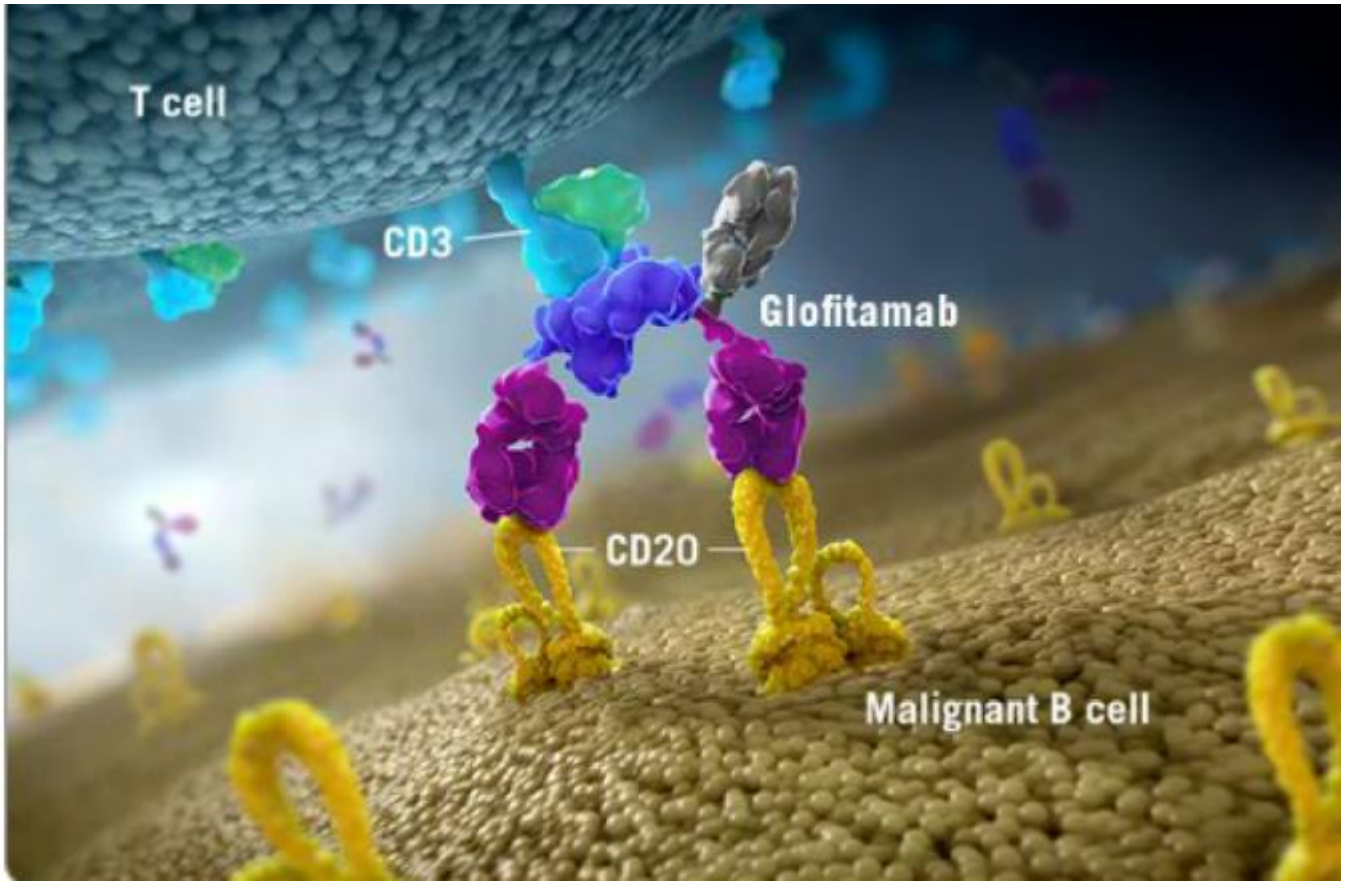
Background

- Glofitamab is a T-cell-engaging bispecific antibody with a novel '2:1' format shown pre-clinically to offer greater avidity, potency, and combinability with other anti-CD20 IgG antibodies than alternative bispecific formats[1]
- Glofitamab SUD, in addition to Gpt, allowed dose escalation up to 30mg to maximise efficacy, while mitigating CRS[2]
- Here, we present updated efficacy data* for the following glofitamab SUD cohorts (D1/D8/target dose from C2D1):
  - 2.5/10/16mg
  - 2.5/10/30mg



*Clinical cut-off date: December 01, 2020.
C, cycle; CRS, cytokine release syndrome; D, day; Gpt, obinutuzumab (G) pretreatment.

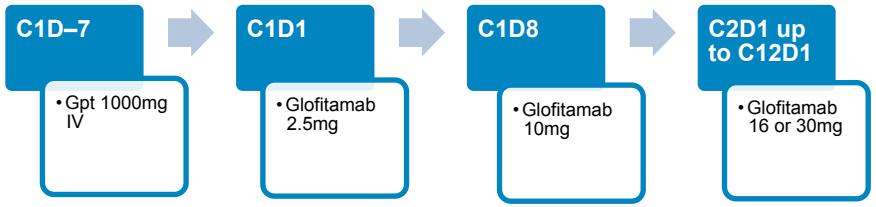
1. Bacac M, et al. Clin Cancer Res 2018;24:4785–97;
2. Hutchings M, et al. J Clin Oncol 2021 (online ahead of print).


T cell
CD3
Glofitamab
CD20
Malignant B cell

NP30179 (NCT03075696): an ongoing Phase I/II dose-escalation and expansion study in R/R NHL

Treatment schedule

- 1000mg Gpt 7 days prior to glofitamab administration
- Glofitamab IV step-up doses on C1D1 and D8 and at target dose from C2D1 (2.5/10/16mg or 2.5/10/30mg)
- C1 was 14-days long; glofitamab was given Q3W thereafter for up to 12 cycles



Clinical cut-off date: 01 December 2020

Key inclusion criteria

- Age: ≥18 years
- Histologically confirmed B-cell NHL expected to express CD20
- ≥1 prior lymphoma treatment
- ≥1 measurable target lesion
- Adequate haematologic, renal and liver functions
- ECOG performance status ≤1

Primary objectives

- Safety, tolerability, pharmacokinetics
- Anti-tumour efficacy[1]
- MTD, optimal biological dose and the RP2D

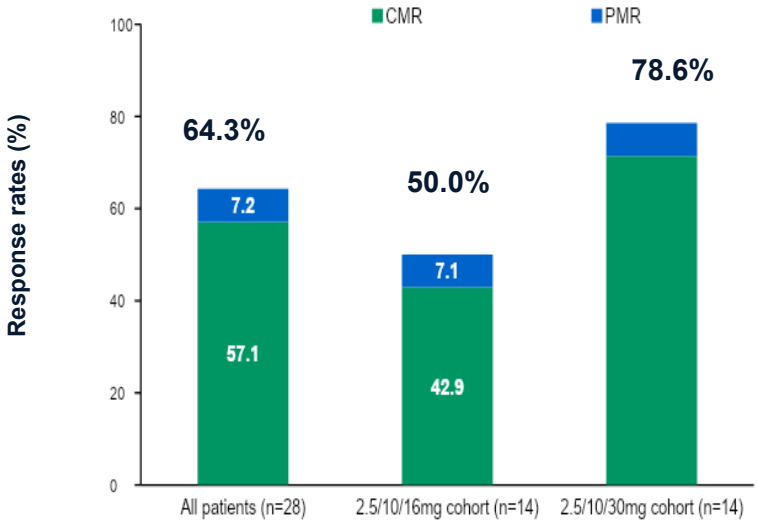
ECOG, Eastern Cooperative Oncology Group; IV, intravenous; MTD, maximum tolerated dose; RP2D, recommended Phase II dose; Q3W, once every 3 weeks.

1. Cheson BD, et al. J Clin Oncol 2014;32:3059–68.

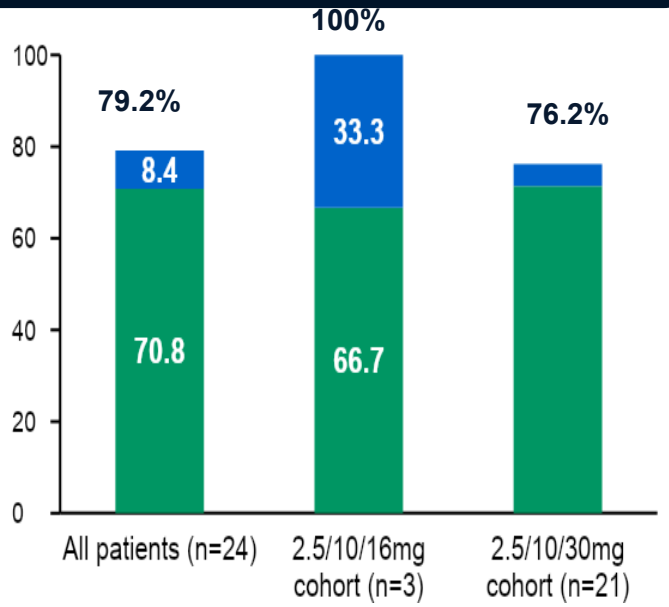
Glofitamab resulted in high response rates

- For aggressive NHL, a trend of improved response was observed at the RP2D (2.5/10/30mg; N=14), with a **CMR rate of 71.4%**
- 4/5 pts (80%) with MCL achieved a CMR

Aggressive NHL



Indolent NHL



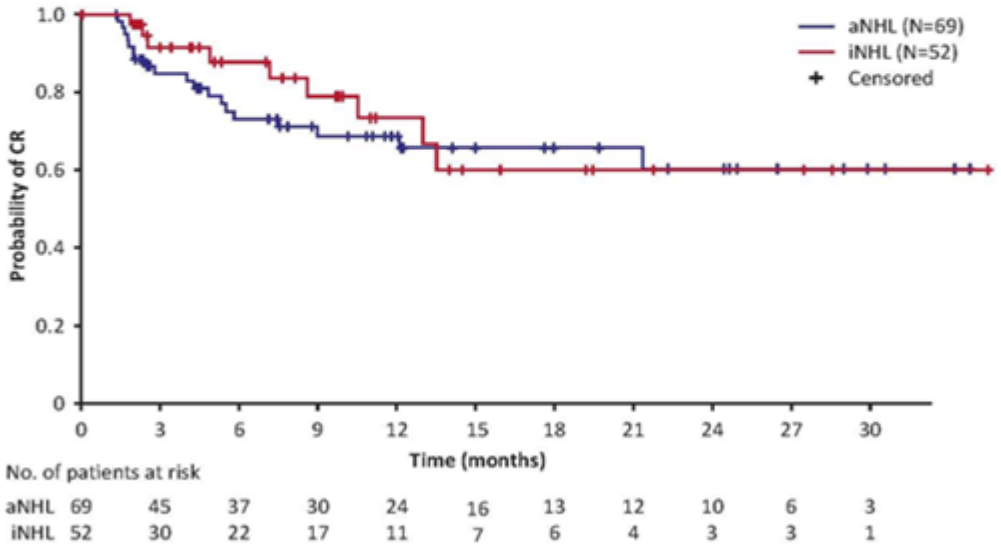
CMR, complete metabolic response; PMR, partial metabolic response.

NP30179 (NCT03075696): an ongoing Phase I/II dose-escalation and expansion study in R/R NHL

Table. Summary of clinical efficacy (efficacy-evaluable population*)

	aNHL, all doses (n=175)	aNHL, RP2D 2.5/10/30mg (n=14)	iNHL, all doses (n=75)
Overall response rate, n (%) [95% CI]	94 (53.7) [46.0, 61.3]	11 (78.6) [49.2, 95.3]	61 (81.3) [70.7, 89.4]
Complete response rate, n (%) [95% CI]	69 (39.4) [32.1, 47.1]	10 (71.4) [41.9, 91.6]	52 (69.3) [57.6, 79.5]
Partial response rate, n (%) [95% CI]	25 (14.3) [9.5, 20.4]	1 (7.1) [0.2, 33.9]	9 (12.0) [5.6, 21.6]

Figure. Duration of complete response (efficacy-evaluable population*)



*The efficacy population includes all patients who have a response assessment performed, or who are still on treatment at the time of their first scheduled response assessment.
aNHL, aggressive non-Hodgkin lymphoma; CI, confidence interval; CR, complete response; iNHL, indolent non-Hodgkin lymphoma; RP2D, recommended Phase II dose.

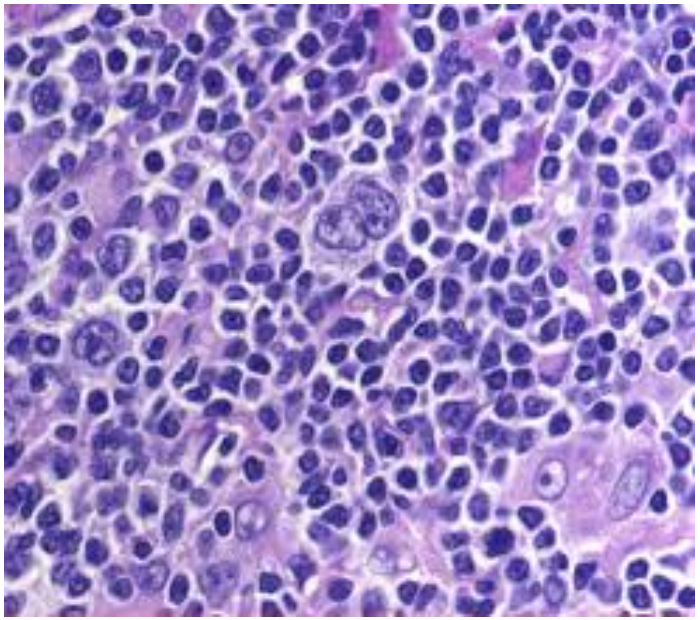
BiTE: esperienza Ravenna

Odronextamab → 2 pazienti: LNH follicolare in relapse

Glofitamab

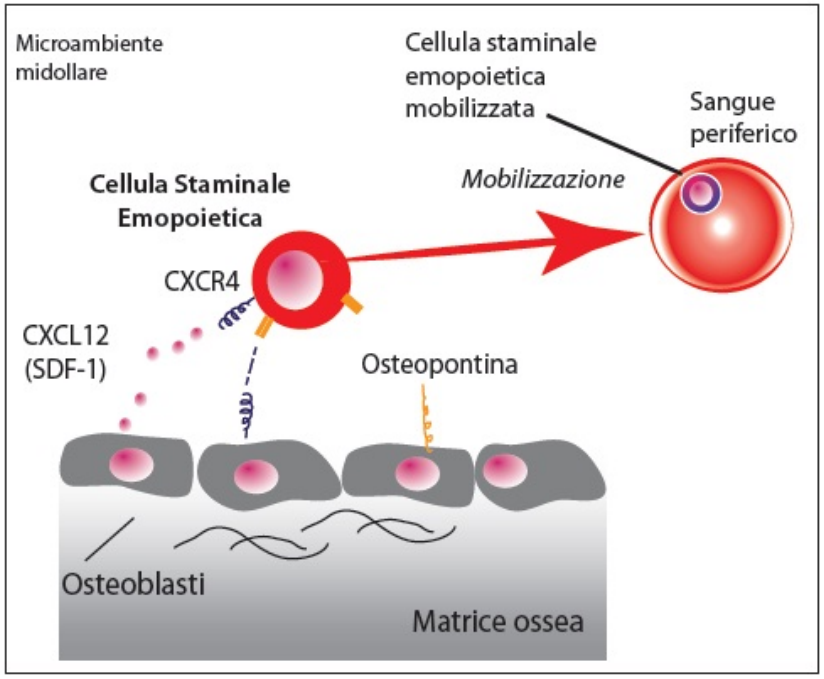
- 4 pazienti DLBCL UNTREATED R-CHOP + BiTE
- 3 pazienti R/R DLBCL
- 1 pz con LNH mantellare in relapse
- 1 pz con LNH follicolare in relapse

Caso clinico



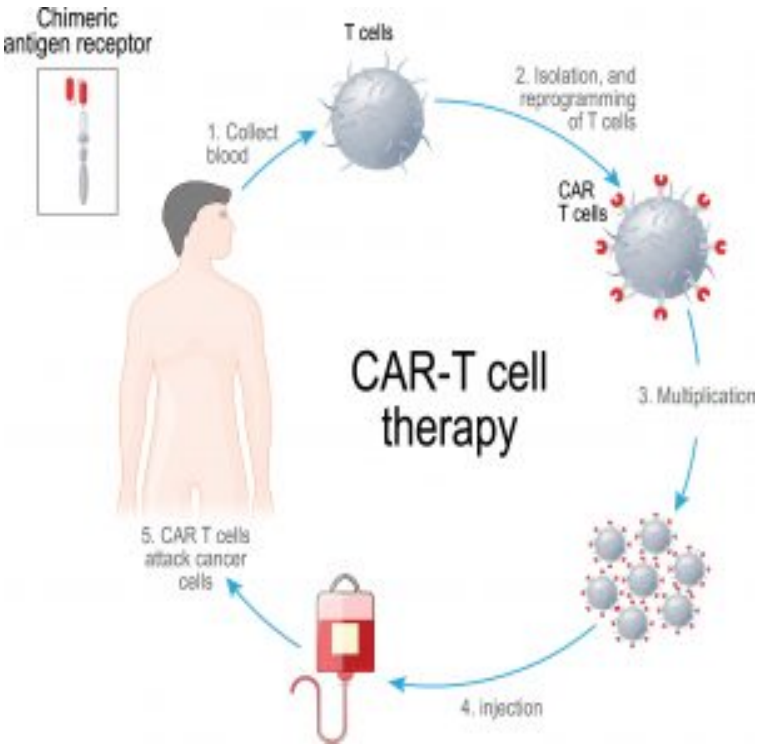
- Femmina 42 aa
- LNH B DLBCL tipo GCB stadio IV B IPI2 (11/2019)
- R-CHOP + rachicentesi medicate con MTX
- PET interim: RC
- PET finale: PD (08/2020)

Caso clinico



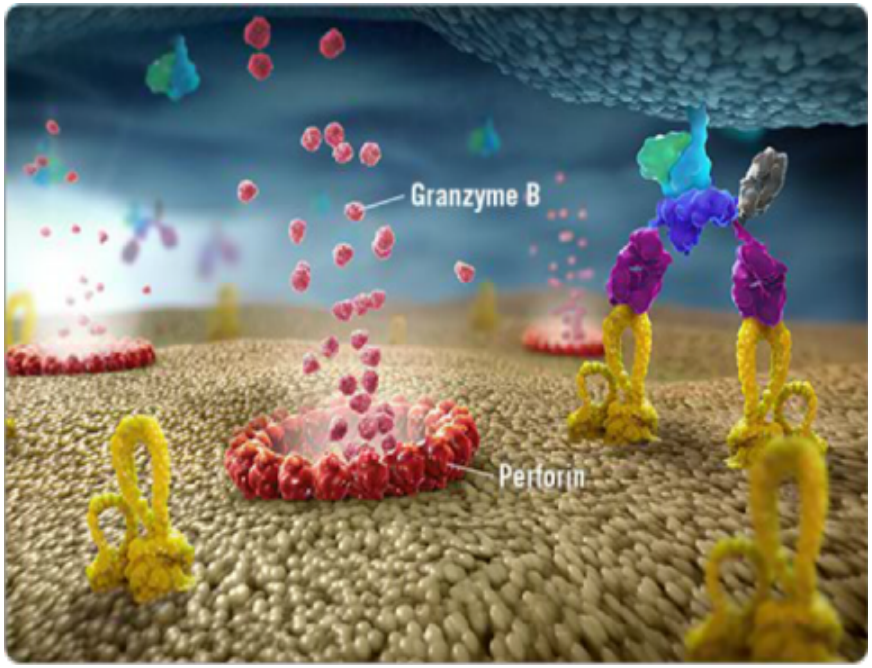
- Schema di salvataggio con R-DHAOX (2 cicli) con raccolta cellule staminali
- PET post terapia RC
- Avviata a ABMT
- Rivalutazione PET post ABMT: PD (03/2021) con localizzazioni sottocutanea, parete toracica ed epatiche

Caso clinico



- Inviata relazione centro di riferimento per terapia con CAR-t
- Non candidabile per ipertransaminasemia e LDH elevato
- Avviata a terapia con Hyper-CVAD (1 ciclo)
  PET rivalutaz: PD

Caso clinico



- Arruolata in protocollo con BiTE (Glofitamab)
- I somm 28/5/2021
- PET post 4 dosi: RC (01/07/2021)
- Avviata a TMO allogenico da cugina

Domande?

Grazie per l'attenzione!